

FAX COVER SHEET

TO: Dr, Anastassios Retzios
RiboGene, Inc.

DATE:

FAX: (510) 731-1775

CC:

FROM: David Haenick

SUBJECT: Emitasol

OF PAGES INCLUDING THIS COVER SHEET: 45

MESSAGE:

Anastassios,

Attached are the draft minutes and timelines from Roberts' Task Force meeting. Please note that we still have to get input from Roberts Canada (Oakville) who will be doing the manufacturing. We can discuss this thoroughly on after your review.

Kind regards,

David

INTEROFFICE MEMORANDUM

TO: Distribution

DATE:

FROM: David Haenick, Ph.D.

**CC: Dr. Petrone
Dr. Tierney**

RE: Emitasol® (Metoclopramide) Nasal Spray Task Force Meeting

The Emitasol Task Force Meeting was held on [redacted] The objectives were to discuss the issues for the CMC, nonclinical, and clinical programs and establish the timelines for the development of the product. In attendance were Ms. Blanset, Ms. Geary, Dr. Kabadi, Mr. Karlan, Dr. Nelson, Dr. Lang, Mr. Raffa, and Ms. Simon.

The development timelines for the CMC, nonclinical, and clinical programs are attached. The key issues are listed below. As this is a draft, please provide your comments to me by [redacted]

CMC

- Choose final formulation – development pharmaceuticals work is in progress.
- IND update – before document can be finalized, the Stability Indicating Method must be validated and the nasal spray formulation must be characterized per FDA guidelines.
- Color change in current formulation - RiboGene has been requested to detect the degradation products responsible for the color change in the current formulation.

Nonclinical

- Due to the change in formulation, determine if additional toxicology studies are needed. Two toxicology consultants with prior FDA experience will be requested to prepare position papers on this issue.

Clinical

- Finalize protocol – FDA has completed their review of the Phase III protocol; their comments will be sent to Roberts during the week of [redacted]
- Choose CRO to conduct Phase III study – budgets are available from two CROs (CPR and Quintiles) and are being reviewed by Roberts Laboratories. Budget from ICON to be provided in [redacted]

Other

- Steering Committee Meeting will be held between Roberts Laboratories and Ribogene on [redacted]

Emitasol Nasal Spray (200 mg/mL) - NDA Development Timeline

Activities	Responsibility	Dates
Formulation Development		
Develop Stability Indicating Analytical Methods	PharmAssist	
Screen prototype formulations and select lead formula	PharmAssist/ CPD/Oakville	
Development Pharmaceutics (spray characterization, etc.)	IBAH/CPD	
Validate Analytical Methods	PharmAssist	
Clinical Supplies		
Prepare formal stability batches to support clinical supplies	Oakville/ CPD	
Stability assessment (1 mo.)	Oakville/CPD	
Manufacture clinical supplies for tox and clinical studies	CPD/ Marketing	
Provide IND update documents to Regulatory	CPD	
File IND update with FDA	Regulatory	
Final Market Formulation		
Identify commercial packaging	CPD/Marketing	
Prepare pilot batches and identify/control critical process	Oakville/CPD	
Stability and data assessment of pilot batches (1 month)	CPD/Oakville	
Manufacture Confirmation Batch(es) (Production filler)*	Oakville	
Manufacture 3 registration/stability batches (Production)	Oakville	
Development Pharmaceutics (spray characterization, etc.)	IBAH/CPD	
Stability and data assessment of registration batches (12 months)	Oakville/CPD	
Development report	CPD	
CMC documentation for NDA	CPD	

* At risk, without one month stability data.

Emitasol® Nasal Spray (200 mg/mL)
Development Timeline (nonclinical and clinical)

Activities	Location	Dates
Nonclinical		
Receive draft rabbit and monkey toxicity reports	Covance	
Issue position paper	Roberts Laboratories	
Send position paper to FDA	Roberts Laboratories	
Clinical		
Bioequivalence assessment	GloboMax	
Finalize protocols	Roberts, RiboGene, GloboMax	
Select CRO to conduct Phase III study	Roberts, RiboGene	
Update Investigator's Brochure	Roberts, GloboMax	
Investigator meeting	Orlando (?)	
Start Phase II study	GloboMax	
Start Phase III study	CRO	
Study reports available	CRO, GloboMax	

D. Haenick

DISTRIBUTION

Ms. Blanset
Mr. Cooke
Ms. Geary
Mr. Howard
Dr. Kabadi
Mr. Karlán
Dr. Nelson
Dr. Lang
Mr. Raffa
Dr. Retzios (RiboGene)
Ms. Simon